



03-01-04

PATENT
674553-2002.1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s) : Vuillard et al.
U.S. Serial No. : 10/627,473
Filing Date : July 25, 2003
For : **CRYSTAL STRUCTURE OF BETA SITE APP
CLEAVING ENZYME (BACE) AND METHODS
OF USE THEREOF**
Group Art Unit : 1632

745 Fifth Avenue
New York, NY 10151

EXPRESS MAIL

Mailing Label Number: EV 195882442 US

Date of Deposit: February 27, 2004

I hereby certify that this paper or fee is being deposited with the
United States Postal Service "Express Mail Post Office to
Addressee" Service under 37 CFR 1.10 on the date indicated above
and is addressed to: **Mail Stop Patent Application,
Commissioner for Patents, P.O. Box 1450, Alexandria, VA
22313-1450.**

Charles B. Jackson

(Typed or printed name of person mailing paper or fee)

(Signature of person mailing paper or fee)

INFORMATION DISCLOSURE STATEMENT

Mail Stop Patent Application
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

The Examiner's attention is respectfully drawn to the enclosed documents listed on the
accompanying PTO form 1449.

As this Information Disclosure Statement is being filed before the mailing of the first Office Action, it is believed that no fee is required for entry of these papers. However, the Commissioner is hereby authorized to charge any such fee, or credit any overpayment to Deposit Account 50-0320.

The filing of this Information Disclosure Statement is not an admission that the documents identified herein constitute prior art to the present application.

Applicants respectfully request that the Examiner considers and makes of record the documents cited herewith and that a copy of Form PTO-1449 be initialed by the Examiner and returned to the undersigned.

Respectfully submitted,

FROMMER LAWRENCE & HAUG LLP
Attorneys for Applicants

Deborah L. Lu

Thomas J. Kowalski
Reg. No. 32,147
Deborah L. Lu
Reg. No. 50,940
(212) 588-0800

Encs. PTO Form 1449
References (49)

Based on Form PTO-1449 (3/90) LIST OF REFERENCES CITED BY APPLICANT (Use several sheets if necessary)	ATTY. DOCKET NO.	SERIAL NO.
	674553-2002.1	10/627,473
	APPLICANT	Vuillard et al.
FILING DATE	GROUP	
July 25, 2003	1632	

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	AA	2004/0014194	01/22/04	Beyer et al.			
	AB						
	AC						
	AD						
	AE						
	AF						
	AG						
	AH						
	AI						

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO
	AJ	EP 0 192 629	08/27/86	Europe				
	AK	EP 0 855 444	07/29/98	Europe				
	AL	WO 00/17369	03/30/00	WIPO				
	AM	WO 00/23576	04/27/00	WIPO				
	AN	WO 00/47618	08/17/00	WIPO				
	AO	WO 00/58479	10/05/00	WIPO				

OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)

	AP		Hussain, I. et al., "Identification of a Novel Aspartic Protease (Asp 2) as β -Secretase," <i>Molecular and Cellular Neuroscience</i> , 14: 419-427, 1999
	AQ		Sinha, S. et al., "Purification and Cloning of Amyloid Precursor Protein β -secretase from Human Brain," <i>Nature</i> , 402: 537-540, 1999
	AR		Lin, X. et al., "Human aspartic protease memapsin 2 cleaves the β -secretase site of β -amyloid precursor protein," <i>PNAS</i> , 97(4): 1456-1460, 2000
	AS		Kopcho, L. et al., "Comparative studies of active site-ligand interactions among various recombinant constructs of human β -amyloid precursor protein cleaving enzyme," <i>Biochemistry and Biophysics</i> , 410: 307-316, 2003
	AT		Mallender, W. et al., "Characterization of Recombinant, Soluble β -Secretase from an Insect Cell Expression System," <i>Molecular Pharmacology</i> , 59(3): 619-626, 2001
	AU		Vassar, R. et al., " β -Secretase Cleavage of Alzheimer's Amyloid Precursor Protein by the Transmembrane Aspartic Protease BACE," <i>Science</i> , 286: 735-741, 1999

EXAMINER

DATE CONSIDERED

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<p>Based on Form PTO-1449 (3/90)</p> <p>LIST OF REFERENCES MAILED BY APPLICANT (Use several sheets if necessary)</p>	ATTY. DOCKET NO.	SERIAL NO.
	674553-2002.1	10/627,473
	APPLICANT	Vuillard et al.
	FILING DATE	GROUP
July 25, 2003		1632

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	AV						
	AW						
	AX						
	AY						
	AZ						
	BA						
	BB						
	BC						
	BD						

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO
	BE	WO 01/00663	01/04/01	WIPO				
	BF	WO 01/00665	01/04/01	WIPO				
	BG	WO 01/23533	04/05/01	WIPO				
	BH	WO 01/55174	08/02/01	WIPO				
	BI	WO 02/25276	03/28/02	WIPO				
	BJ	WO 02/053594	07/11/02	WIPO				

OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)

	BK		Marston, F. et al., "Solubilization of Protein Aggregates," <i>Methods in Enzymology</i> , 182(20): 264-276, 1990				
	BL		Burton, S. et al., "Refolding human serum albumin at relatively high protein concentration," <i>Eur. J. Biochem.</i> , 179: 379-387, 1989				
	BM		Goldberg, M. et al., "Non-detergent sulphobetaines: a new class of molecules that facilitate <i>in vitro</i> protein renaturation," <i>Folding & Design</i> , 1: 21-27, 1995				
	BN		Huxtable, S. et al., "Renaturation of 1-Aminocyclopropane-1-carboxylate Synthase Expressed in <i>Escherichia coli</i> in the Form of Inclusion Bodies into a Dimeric and Catalytically Active Enzyme," <i>Protein Expression and Purification</i> , 12: 305-314, 1998				
	BO		Wei, X. et al., "Expression, Purification and Activity Measurement of Soluble BACE Protein in <i>E.coli</i> ," <i>Acta Biochimica et Biophysica Sinica</i> , 34(4): 498-501, 2002				
	BP		Fischer, F. et al., "The disulphide bonds in the catalytic domain of BACE are critical but not essential for amyloid precursor protein processing activity," <i>Journal of Neurochemistry</i> , 80: 1079-1088, 2002				

EXAMINER	DATE CONSIDERED
----------	-----------------

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<p>Based on Form PTO-1449 (3/90)</p> <p>FEB 27 2004</p> <p>LIST OF REFERENCES CITED BY APPLICANT (Use several sheets if necessary)</p>			ATTY. DOCKET NO.		SERIAL NO.		
			674553-2002.1		10/627,473		
			APPLICANT				
			Vuillard et al.				
			FILING DATE		GROUP		
			July 25, 2003		1632		
U.S. PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	BQ						
	BR						
	BS						
	BT						
	BU						
	BV						
	BW						
	BX						
FOREIGN PATENT DOCUMENTS							
		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION
							YES
	BY	WO 02/088101	11/07/02	WIPO			
	BZ	WO 03/012089	02/13/03	WIPO			
	CA	WO 03/072733	09/04/03	WIPO			
	CB	WO 96/40885	12/19/96	WIPO			
	CC	WO 98/26059	06/18/98	WIPO			
	CD	WO 99/31236	06/24/99	WIPO			
	CE	WO 99/64587	12/16/99	WIPO			
OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)							
	CF		Kurimoto, E. et al., "In Vitro Refolding of Porcine Pepsin Immobilized on Agarose Beads," <i>J. Biochem.</i> , 130, 295-297, 2001				
	CG		Hong, L. et al., "Crystal Structure of Memapsin 2 (β-Secretase) in Complex with an Inhibitor OM00-3," <i>Biochemistry</i> , 41: 10963-10967, 2002				
	CH		Ghosh, A. et al., "Design of Potent Inhibitors for Human Brain Memapsin 2 (β-Secretase)," <i>J. Am. Chem. Soc.</i> , 122: 3522-3523, 2000				
	CI		Greer, J. et al., "Application of the Three-Dimensional Structures of Protein Target Molecules in Structure-Based Drug Design," <i>Journal of Medicinal Chemistry</i> , 37(8): 1035-1054, 1994				
	CJ		Verlinde, C. et al., "In search of new lead compounds for trypanosomiasis drug design: A protein structure-based linked-fragment approach," <i>Journal of Computer-Aided Molecular Design</i> , 6: 131-147, 1992				
	CK		Jones, G. et al., "Docking small-molecule ligands into active sites," <i>Current Opinion in Biotechnology</i> , 6: 652-656, 1995				
EXAMINER				DATE CONSIDERED			
<p>* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</p>							

Based on Form PTO-1449 (3/90) LIST OF REFERENCES CITED BY APPLICANT (Use separate sheet if necessary)	ATTY. DOCKET NO.	SERIAL NO.
	674553-2002.1	10/627,473
	APPLICANT	Vuillard et al.
	FILING DATE	GROUP
July 25, 2003		1632

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	CL						
	CM						
	CN						
	CO						
	CP						

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO
	CQ							
	CR							
	CS							
	CT							

OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)

	CU		Tung, J. et al., "Design of Substrate-Based Inhibitors of Human β -Secretase," <i>J. Med. Chem.</i> , 45(2): 259-262, 2002
	CV		Horn, R. et al., "Design of Synthesis of Statine-Based Cell-Permeable Peptidomimetic Inhibitors of Human β -Secretase," <i>J. Med. Chem.</i> , 46: 1799-1802, 2003
	CW		Hong, L. et al., "Structure of the Protease Domain of Memapsin 2 (β -Secretase) Complexed with Inhibitor," <i>Science</i> , 290: 150-53, 2000 (XP-002161207)
	CX		Turner, R. et al., "Subsite Specificity of Memapsin 2 (β -Secretase): Implications for Inhibitor Design," <i>Biochemistry</i> , 40(34): 10002-10006, 2001 (XP-001095820)
	CY		Ghosh, A. et al., "Structure-Based Design: Potent Inhibitors of Human Brain Memapsin 2 (β -Secretase)," <i>J. Med. Chem.</i> , 44: 2865-2868, 2001 (XP-002213861)
	CZ		Abagyan, R. et al., "High-throughput docking for lead generation," <i>Current Opinion in Chemical Biology</i> , 5: 375-382, 2001 (XP-001156102)
	DA		Ermoloeff, J. et al., "Proteolytic Activation of Recombinant Pro-memapsin 2 (Pro- β -secretase) Studied with New Fluorogenic Substrates," <i>Biochemistry</i> , 39: 12450-12456, 2000 (XP-002162928)
	DB		Shi, X. et al., "The Pro Domain of β -Secretase Does Not Confer Strict Zymogen-like Properties but Does Assist Proper Folding of the Protease Domain," <i>The Journal of Biological Chemistry</i> , 276(13): 10366-10373, 2001 (XP-002265190)
	DC		Vassar, R., "The β -Secretase, BACE," <i>Journal of Molecular Neuroscience</i> , 17: 157-170, 2001 (XP-009023186)
	DD		Bruinzel, W. et al., "Recombinant insect cell expression and purification of human β -secretase (BACE-1) for X-ray crystallography," <i>Protein Expression and Purification</i> , 26: 139-148, 2002 (XP-002265191)
	DE		Turner, R. et al., "Substrate Specificity of Memapsin 2 (β -Secretase): Basis for Inhibitor Drug Design for Alzheimer's Disease," <i>FASEB Journal</i> , 15: A538, 2001 (Abstract)

EXAMINER	DATE CONSIDERED

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.